REMARKS

I. The Subject Matter of the Claims

In general, the subject matter of the claims relates to methods for detecting ICAM-4 in a sample and to monoclonal antibodies specific for human ICAM-4 protein.

II. Priority

The Examiner asserts that priority for claim 27 is not found in the parent specification. Applicants respectfully disagree. Support for an antibody that is specifically immunoreactive with ICAM-4 and ICAM-4 variants is disclosed at page 7, lines 4-5, and was also found in parent application no. 08/245,295, now U.S. Patent No. 5,700,568, filed May 18, 1994.

Also, the current specification and priority document contemplate use of binding proteins that are specific for ICAM-4 at page 8, lines 2-5. As such, the prior applications fully support claim 27, as amended, and the claim does not add new matter.

III. The Objections to the Specification

Applicants note the Examiner's objection that reference to U.S. patent applications must be removed and/or updated to reflect their current status. Applicant submits that amendments to the specification obviate the Examiner's rejection. Additionally, to the best of Applicants' knowledge no other errors exist in the text of the specification.

IV. Support for the Claims

Support for amendment to claim 27 to recite an ICAM-4 encoded by the polynucleotide of SEQ ID NO: 27, a polynucleotide that encodes SEQ ID NO: 28 or a polynucleotide sequence that hybridizes to said sequence is found at page 37, lines 5-7. Support for the term specifically immunoreactive is found at page 7, lines 4-5. Support for a fragment of human ICAM-4 polypeptide is found, for example, at page 6, lines 9-13, and at page 7, lines 18-21, which discloses ICAM-4 polypeptide variants and fragments. Additional support is disclosed at page 40, lines 25-27, which

discloses fusion proteins made with ICAM-4 polypeptide fragments, and at page 45, lines 16-20 which describe antibody binding of ICAM-4 fragments.

The amendment includes no new matter.

V. Patentability Arguments

A. The Rejections of Claims 23-27 Under 35 U.S.C. §112, First Paragraph, May Properly Be Withdrawn

The examiner rejects claims 23-26 under 35 U.S.C. §112, first paragraph, as assertedly not enabled by the specification. The Examiner contends that statements in the specification that hybridomas 179H and 179I have been deposited is not sufficient for written description, and that a declaration that the hybridomas were deposited under the terms of the Budapest Treaty is required.

Applicants submit herewith a Statutory Declaration executed by a representative of the Applicants indicating that the hybridomas have been deposited under the correct terms. Copies of the deposit receipt for hybridomas 179H and 179I issued by the American Type Culture Collection are also submitted.

The Examiner rejects claim 27 under 35 U.S.C. §112, first paragraph, as assertedly lacking written description, objecting to the phrase "antibody that specifically binds." The Examiner asserts that the Applicants have defined the term "specifically binds" as having exclusive binding to only a particular antigen, and that this is inconsistent with the art-recognized teaching of antibody binding. The Examiner contends that because Applicants have not tested the monoclonal antibody against every epitope in nature, it cannot be deemed specific for only ICAM-4.

Applicants respectfully disagree, and submit that it is well-known in the art what is meant by referring to antibody binding specificity. Applicants previously referred to an art-accepted manual for producing monoclonal antibodies, Harlow *et al*, "Antibodies: A Laboratory Guide," (1988) to obtain their definition of "specific binding". Applicants stated previously that the "Harlow *et al.*" book sets out that a specifically binding antibody is one that only recognizes the appropriate antigen (Harlow *et al.*, Ch. 5) and has a defined, unique specificity (Harlow *et al.*, Ch. 6,

"Monoclonal Antibodies"). See Applicants' "Response to Restriction Requirement and Amendment", July 15, 2003, page 3.

Without paraphrasing, Harlow *et al*, at chapter 1, page 2, defines that "the specificity of the immune response is controlled by a simple mechanism - one cell recognizes one antigen." Harlow further states when discussing monoclonal antibodies that "hybridomas maintained *in vitro* continue to secrete antibodies with a defined specificity (*emphasis added*). Antibodies that are produced by hybridomas are known as monoclonal antibodies," (Harlow *et al.*, "Antibodies: A Laboratory Guide," (Chapter 6, page 141, 1988). Harlow also states that "the production of monoclonal antibodies allows the isolation of reagents with a unique, chosen specificity" (Harlow, Chapter 6, page 141). Thus, the Applicants' definition is consistent with that in the art.

Moreover, page 8, lines 2-5, of the specification clearly set out what Applicants mean by specific ICAM-4 binding by an antibody, "i.e. non-reactive with the ICAM-1, -2, and ICAM-R intracellular adhesion molecules to which ICAM-4 is structurally related." Applicants recognize that these proteins share varied degrees of structural homology (see specification page 37, line 23 to page 38, line 3), and defines an ICAM-4 specific biding protein (page 8, lines 2-5) as one that does not interact with these structurally similar proteins.

The claimed antibody is therefore one that is immunospecific for ICAM-4 as defined in the specification, and the Applicants maintain that this term is understood in the art. Further, an antibody that cross-reacts with another molecule, specifically a structurally related molecule as stated above, lies outside the scope of the claim. In view of the arguments above, Applicants submit that the rejection of claim 27 under 35 U.S.C. § 112, first paragraph, may properly be withdrawn.

B. The Rejection of Claims 23-27 Under 35 U.S.C. §112, Second Paragraph, May Properly Be Withdrawn

The examiner rejects claim 27 as assertedly indefinite in its recitation of "human ICAM-4." Applicants submit that amendment to the claim to add sequence identifiers for human ICAM-4 obviates the Examiner's rejection.

C. The Rejection of Claim 27 Under 35 U.S.C. §102 (b), May Properly Be Withdrawn

The Examiner rejects claim 27 under 35 U.S.C. §102 (b) as being directed to subject matter assertedly anticipated by the disclosure of Oka, in light of Yoshihara. The Examiner has asserted that the cited references disclose that the telencephalin proteins described by Oka and Yoshihara are homologs of the present ICAM-4, and the Examiner contends that because the polyclonal anti-telenchephalin anti-sera disclosed by Oka binds to telencephalin from several species, this suggests that the monoclonal antibody specific for rabbit telencephalin, as disclosed by Oka, will necessarily bind to the presently disclosed ICAM-4.

For a reference to anticipate, that single reference must disclose each and every limitation of the claimed invention. Further, MPEP 2131.01 (III) states that to serve as an anticipation when the reference is silent about any asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.

Regardless of the asserted cross-reactivity ascribed to the disclosed polyclonal anti-sera, Oka indicated that the rabbit monoclonal antibody is not useful for isolating other telencephalin proteins because it fails to cross-react with any other species' telencephalin (see Oka, page 94, first paragraph). Given this limitation, which is clearly expressed by the Oka reference, one cannot infer that the disclosed antibody will necessarily bind to the human protein. In fact, Oka refutes the Examiner's assertion. Oka gives no indication which epitope in the rabbit telencephalin protein the monoclonal antibody 2716A binds, but the failure of this monoclonal antibody to cross-react with orthologs of the rabbit protein suggests distinct region(s) in the rabbit protein not found in orthologs. Thus, the Oka monoclonal antibody specific for rabbit telencephalin cannot anticipate the subject matter of a claim reciting a monoclonal antibody that binds to the human ICAM-4 disclosed herein.

The Examiner further rejects claim 27 under 35 U.S.C. §102(b) as assertedly unpatentable in view of Bailly. Bailly describes a polypeptide designated as an LW antigen, which Bailly refers to as ICAM-4. Although the proteins have the same name, they are different polypeptide sequences (Compare, for example, SEQ ID NO: 28 disclosed herein to Figure 2 in Bailly (1994, *supra*)). Applicants submit that amendment to claim 27 to include sequence identifiers of ICAM-4 obviates the Examiner's rejection.

D. The Rejection of Claim 27 Under 35 U.S.C. §103(a), May Properly Be Withdrawn

Claim 27 was rejected under 35 U.S.C. §103(a) as assertedly rendered obvious by the disclosure of Oka, in view of the disclosure of Yoshihara, and further in view of Goding. The Examiner asserts that the cited references disclose antibodies that would "be reasonably expected to bind human telencephalin." The Examiner asserts that it would have been obvious for a worker of skill to use the polyclonal antibody disclosed by Oka to isolate human telencephalin, and once isolated it would be assertedly obvious to produce anti-human telencephalin monoclonal antibodies.

Applicants respectfully disagree. The present application is the first disclosure of a human ICAM-4, which is defined by amino acid sequence SEQ ID NO: 28 in the specification. To the extent that the worker of ordinary skill might have speculated that a human ortholog might exist, this same worker certainly could not have speculated that such human protein would be encoded by the claimed polynucleotide sequence, or that it would be encoded by a polynucleotide that hybridizes to the recited sequence.

Moreover, because Oka discloses a monoclonal antibody that fails to cross-react with proteins from other species, the reference suggests that purportedly related proteins may not possess conserved sequence similarity. Absent knowledge of ICAM-4's existence, and in light of disclosure of Oka's monoclonal antibody that does not cross-react across species, the worker of ordinary skill would not have a reasonable expectation of success at isolating the ICAM-4 molecule of SEQ ID NO: 27 and 28 identified herein, and subsequently making monoclonal antibodies that specifically bind that polypeptide sequence.

Thus, Applicants submit that the Examiner's rejection of claim 27 under 35 U.S.C. §103 (a) as obvious in view of Oka, in light of Yoshihara and Goding, may properly be withdrawn.

E. The Rejection of Claim 27 under the Doctrine of Obviousness-type Double Patenting May Properly be Withdrawn

The Examiner rejects claim 27 based on non-statutory obviousness-type double patenting, as allegedly unpatentable over claims 1-6 of U.S. Patent No. 5,773,293 (hereinafter "the '293 patent"). The Examiner states that the claim, directed to a monoclonal antibody that specifically binds ICAM-4, is assertedly not patentably distinct from, and is assertedly anticipated by disclosure of the monoclonal antibodies in the '293 patent.

Applicants enclose herewith a terminal disclaimer with respect to U.S. Patent No. 5,773,293, which obviates the Examiner's rejection.

VI. Conclusion

In view of the amendments and remarks made herein, Applicants submit that claims 23-27 are in condition for allowance and respectfully request expedited notification of the same.

Respectfully submitted,

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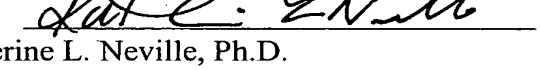
By 

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